

ORIGINAL ARTICLES

Does aspirin affect the rate of cataract formation? Cross-sectional results during a randomised double-blind placebo controlled trial to prevent serious vascular events

UK-TIA Study Group*

Abstract

A total of 2435 patients with transient ischaemic attack or minor ischaemic stroke were entered into the UK-TIA aspirin trial and randomised to treatment with aspirin 1200 mg/day, aspirin 300 mg/day, or placebo. At a single point in time during the trial patients were examined ophthalmoscopically for evidence of cataracts. The length of time that each patient had been participating in the trial at the time of ophthalmic examination varied from 1 to 5 years. The prevalence of cataracts was similar in patients allocated aspirin and patients allocated placebo irrespective of the length of time that they had been in the trial. These findings suggest that aspirin taken in a dose of 300 to 1200 mg daily for a few years does not prevent cataracts.

Aspirin is a remarkable preparation; it relieves our aches and pains, reduces fever, lowers the risk of serious vascular events in patients with symptomatic cardiac or cerebral ischaemia by about a quarter,¹ and it is widely available, inexpensive, and relatively non-toxic. Furthermore it has been claimed recently that aspirin may protect against cataract, the world's leading cause of blindness.²⁻¹⁰ However aspirin has not been generally accepted as an effective cataract prophylactic because of conflicting data from several other studies.¹¹⁻¹⁶ In view of the uncertainty about the effect, if any, of aspirin in preventing blindness, and the implications if it were effective, we took an unusual opportunity to test the hypothesis that aspirin reduces the incidence of cataract formation by examining patients towards the end of the United Kingdom Transient Ischaemic Attack (UK-TIA) aspirin trial.¹⁷ If aspirin prevents cataract then we would anticipate a divergence of cataract prevalence between those allocated aspirin and those allocated placebo, becoming more marked the longer the patients had been in the trial.

Methods

Between 25 July 1979 and 8 October 1985 a total of 2435 patients with a recent transient ischaemic

attack (TIA) or minor ischaemic stroke entered the UK-TIA aspirin trial and were allocated at random to receive aspirin 600 mg twice daily, aspirin 300 mg once daily, or matching placebo. The trial methods have been published elsewhere.¹⁷ During 1984/85 surviving patients still attending hospital for follow-up ($n=1889$) were assessed for evidence of cataract formation; patients were asked whether they had ever been told that they had a cataract and whether they had undergone cataract removal and, if so, when. The patient was then examined by the neurologist using an ophthalmoscope and cataracts were classified as present or absent.

Results

Table 1 shows the prevalence of cataracts detected ophthalmoscopically in one or both eyes in each of the three treatment groups, the number of cataract extractions performed during the study period up until 1985 among patients in each of the treatment groups, and the number of patients with ophthalmological evidence of cataracts according to the treatment received and the time from randomisation - that is, the duration of treatment. The relative risk of developing ophthalmological evidence of cataracts according to the treatment received and the time from randomisation is illustrated in Figure 1. No significant protective effect is apparent. A separate analysis, excluding those patients who had stopped their trial medication, revealed very similar results.

Discussion

This study is an example of opportunistic research. After more than 2000 patients with non-disabling cerebral or ocular ischaemia had been randomised to treatment with aspirin or placebo they were examined by their neurologist at a single point in time during follow-up to determine whether they had ophthalmoscopic evidence of cataracts or not.

DIAGNOSIS OF CATARACT

The neurologists, who were well trained in the

*Collaborators listed in reference 17.

Correspondence to:
Dr Graeme J Hankey,
Department of Clinical
Neurosciences, Western
General Hospital, Crewe
Road, Edinburgh EH4 2XU.

Accepted for publication
20 September 1991

Table 1

	Treatment			95% Confidence interval	Treatment			95% Confidence interval
	Any aspirin (n=1268)	Placebo (n=621)	Odds ratio		Aspirin 300 mg (n=624)	Aspirin 1200 mg (n=644)	Odds ratio	
Cataract (ophthalmoscopic)								
Yes	162 (13%)	81 (13%)	1.0	(0.8 to 1.4)	76 (12%)	86 (13%)	0.9	(0.6 to 1.2)
No	1103	539			547	556		
No eye	3	1			1	2		
Cataract extraction (after randomisation)	4	3			0	4		
	Any aspirin (n=162)	Placebo (n=81)	χ^2 (df=5)	p value	Aspirin 300 mg (n=76)	Aspirin 1200 mg (n=86)	χ^2 (df=5)	p value
Time from randomisation to ophthalmoscopic assessment in patients with cataracts (years)								
0-1	20	9			9	11		
1-2	27	11			14	13		
2-3	27	20	3.35	0.65	11	16	2.73	0.74
3-4	36	13			20	16		
4-5	23	13			11	12		
5+	29	15			11	18		

use of an ophthalmoscope and the interpretation of what was seen, were asked to simply state whether a cataract was present or not in either eye based on the appearance of a definite silhouette of the opacity against the background of the red reflex. Standardised diagnostic criteria were not applied because we were not (and still are not) aware of any internationally accepted diagnostic criteria that could be applied easily in a neurology outpatient clinic. Although there may have been some inaccuracies in the diagnosis of cataract these are unlikely to have biased the results because the examiners were not aware – that is, they were ‘blind’ – of the treatment allocated to the patient. It is likely therefore that any inaccuracies in diagnosis were equally distributed in the aspirin-treated and the placebo-treated groups. Furthermore if the prevalence of cataracts (13%) diagnosed in this population of patients (of mean age 60 (SD 9) years) is compared with the prevalence of cataracts in the 2675 individuals in the Framingham eye study the results were similar. In the Framingham eye study the prevalence of cataracts increased from 4.6% in those between the ages of 52 and 64 years to 46% in those between 75 and 85 years.¹⁸

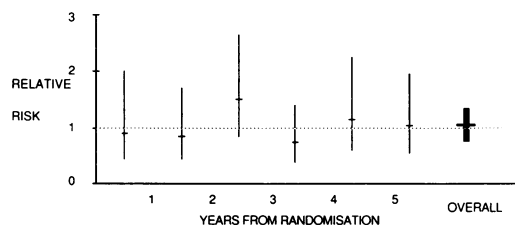


Figure 1 Relative risk (placebo:aspirin) of having ophthalmoscopic evidence of cataracts according to treatment with placebo or aspirin and the time from randomisation to either placebo or aspirin therapy. If the relative risk is greater than 1.0 the prevalence of cataract in patients allocated placebo is greater than in those allocated aspirin. The short horizontal line for each year represents the estimated relative risk and the vertical line the 95% confidence interval of the estimate. The thick horizontal and vertical lines on the right indicate the estimate and its 95% confidence interval respectively of the overall relative risk. As all of the 95% confidence intervals (vertical lines) overlap with a relative risk of 1.0 (dotted line) the result is not statistically significant at the $p=0.05$ level.

FOLLOW-UP

The time interval between randomisation – that is, entry into the study – and the ophthalmological examination for cataracts varied among the patients from less than 1 to more than 5 years. It is not known whether any cataracts had developed before or after treatment was commenced with aspirin or placebo. However the process of randomisation protects against systematic bias in treatment allocation.

RESULTS

If aspirin has a protective effect on cataract formation it would be expected, in a study of this kind, that the relative risk of having a cataract would be approximately one within the first year of randomisation and, as the time interval from randomisation to assessment increased, the prevalence of cataract formation in the placebo group would gradually increase compared with the aspirin-treated group. This was not the case; there was no significant change in the relative risk over the first 5 years of treatment and no evidence to suggest a time-dependent effect.

CONCLUSION

The limitations of this study are not that the diagnosis of cataract was based upon a relatively crude method (an ophthalmoscope) but that the primary measure of outcome (cataract formation) was assessed at a single point in time only and that the number of patients with cataracts was fairly small, leading to imprecise estimates of relative risk with fairly wide confidence intervals and hence the possibility of a ‘false negative’ result. Nevertheless the results do not support the hypothesis that 300–1200 mg daily aspirin, taken for a few years, is an effective cataract prophylactic.

This paper was prepared by Dr Graeme Hankey, Dr Susan Richards and Professor Charles Warlow.

The UK-TIA aspirin trial was supported by a grant from the Medical Research Council and the European Aspirin Foundation, and Dr Hankey received a grant from the Chest Heart and Stroke Association. We are grateful for helpful comments on the manuscript by Dr P Sandercock, Mr R Peto and Ms B Farrell.

- 1 Antiplatelet Trialists' Collaboration. Secondary prevention of vascular disease by prolonged antiplatelet treatment. *BMJ* 1988; **296**: 320-31.
- 2 Cotlier E. Rheumatoid arthritis and cataract surgery. *Int Ophthalmol* 1980; **2**: 127-9.
- 3 Cotlier E, Sharma YR. Aspirin and senile cataracts in rheumatoid arthritis. *Lancet* 1981; **i**: 338-9.
- 4 Cotlier E. Senile cataracts: evidence of acceleration by diabetes and deceleration by salicylate. *Can J Ophthalmol* 1981; **16**: 113-8.
- 5 Cotlier E, Sharma YR, Niven T, Brescia M. Distribution of salicylate in lens and intraocular fluids and its effect in cataract formation. *Am J Med* 1983; **74**: 83-90.
- 6 Crompton M, Rixon KC, Harding JJ. Aspirin prevents carbamylation of soluble lens proteins and prevents cyanate-induced phase separation opacities in vitro: a possible mechanism by which aspirin could prevent cataract. *Exp Eye Res* 1985; **40**: 297-311.
- 7 Rao GN, Lardis MP, Cotlier E. Acetylation of lens crystallins: a possible mechanism by which aspirin could prevent cataract formation. *Biochem Biophys Res Comm* 1985; **128**: 1125-32.
- 8 Van Heyningen R, Harding JJ. Do aspirin-like analgesics protect against cataract? A case-control study. *Lancet* 1986; **i**: 1111-3.
- 9 Harding JJ, Van Heyningen R. Drugs, including alcohol, that act as risk factors for cataract, and possible protection against cataract by aspirin-like analgesics and cyclo-penthiiazide. *Br J Ophthalmol* 1988; **72**: 809-14.
- 10 Swamy MS, Abraham EC. Inhibition of lens crystallin glycation and high molecular weight aggregate formation by aspirin in vitro and in vivo. *Invest Ophthalmol Vis Sci* 1989; **30**: 1120-6.
- 11 Seigel D, Sperduto RD, Ferris FL III. Aspirin and cataracts. *Ophthalmology* 1982; **89**: 47-8A.
- 12 Seigel D, Sperduto RD, Ferris F. Is ASA therapy for cataract justified? *Can J Ophthalmol* 1982; **1**: 135-6.
- 13 Kewitz H, Nitz M, Gaus V. Aspirin and cataract. *Lancet* 1986; **ii**: 689.
- 14 West SK, Munoz BE, Newland HS, Emmett EA, Taylor HR. Lack of evidence for aspirin use and prevention of cataracts. *Arch Ophthalmol* 1987; **105**: 1229-31.
- 15 Peto R, Gray R, Collins R, et al. A randomised trial of the effects of prophylactic daily aspirin among male British doctors. *BMJ* 1988; **296**: 313-6.
- 16 Paganini-Hill A, Chao A, Ross RK, Henderson BE. Aspirin use and chronic diseases: a cohort study of the elderly. *BMJ* 1989; **299**: 1247-50.
- 17 UK-TIA Study Group. United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: interim results. *BMJ* 1988; **296**: 316-20.
- 18 Kini MM, Leiowitz HM, Colton T, Nickerson RJ, Ganley J, Dawber TR. Prevalence of senile cataract, diabetic retinopathy, senile macular degeneration, and open-angle glaucoma in the Framingham eye study. *Am J Ophthalmol* 1978; **85**: 28-34.
- 19 Gardner MJ, Altman DG, eds. In: *Statistics with confidence*. Belfast, Universities Press. *BMJ*, 1989.

FIFTY YEARS AGO

Tobacco Amblyopia

In hospital practice, in which tobacco amblyopia is common, the patients do not come from the section of the population in which hard drinking by both sexes, often supported by cheap alcohol, is frequent. These people come to the medical and surgical outpatient departments and exhibit the clinical picture of chronic alcoholism; they do not come to the eye department complaining of impaired vision. If alcohol were an important factor toxic amblyopia would be much more common in women than it is. Tobacco amblyopes are frequently moderate or light drinkers and are often teetotalers.

Br J Ophthalmol 1942; **26**: 43.



Does aspirin affect the rate of cataract formation? Cross-sectional results during a randomised double-blind placebo controlled trial to prevent serious vascular events. UK-TIA Study Group.

Br J Ophthalmol 1992 76: 259-261
doi: 10.1136/bjo.76.5.259

Updated information and services can be found at:
<http://bjo.bmj.com/content/76/5/259>

	<i>These include:</i>
References	Article cited in: http://bjo.bmj.com/content/76/5/259#related-urls
Email alerting service	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>